UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/342,993	06/29/99	POIRIER	J 08523/005002

EXAMINER	
TU, S	
ART UNIT	PAPER NUMBER
1653	4

HM12/0413

KRISTINA BIEKER BRADY
CLARK AND ELBING LLP
176 FEDERAL STREET
BOSTON MA 02110

DATE MAILED: 04/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/342,993	Applicant(s) POIRIER, JUDES	
	Examiner Stephen Tu	Art Unit 1653	

-- Th MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 5 February 2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/342,993 is acceptable and a CPA has been established. An action on the CPA follows.

Priority

2. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(a)-(d) based upon an application filed in Great Britain on 27 April 1994. A claim for priority under 35 U.S.C. 119(a)-(d) cannot be based on said application, since the United States application was filed more than twelve months thereafter.***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 6 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of diseases responsive to cholinomimetic drugs, such as Alzheimer's disease, does not reasonably provide enablement for all diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, are set forth in *In re Wands*, 8 USPQ2d 1400, at 1404 (CAFC, 1988). These factors include: (1) the nature of the invention, (2) the state of the prior art, (3) the relative level of skill of those in the art, (4) the predictability of the art, (5) the

breadth of the claims, (6) the amount of direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary.

The specification discloses the cholinomimetic therapies, and in particular the drug tacrine. Tacrine is a reversible acetylcholinesterase inhibitor that prevents the degradation of endogenously released acetylcholine. While the efficacy of this drug has been established with respect to the treatment of Alzheimer's disease, it is not evident from the prior art or from the specification that this drug would be equally effective in the treatment of other diseases.

However, Claim 6 recites "A method... for the treatment of a disease,...." The claim as written is not limited to the treatment of diseases that would be responsive to cholinomimetic drugs or even neurodegenerative diseases. Thus, the specification fails to provide any working examples or guidance on the use of cholinomimetic drugs in the treatment of other diseases. In view of the forgoing, it is the position of the Examiner that undue experimentation would be required on the by one of ordinary skill in the art to practice the invention with respect to diseases other than neurodegenerative diseases, particularly those responsive to cholinomimetic drugs.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-3 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1, and claims dependent therefrom, are directed to a method of identifying human subjects that would be responsive to a cholinomimetic drug. The method comprises "determining the number of copies of apoE4 gene alleles in said subject," however the

claims do not set forth the steps that would be taken to determine the number of apoE4 alleles in a subject. Furthermore, the use of "respond" in "respond to a cholinomimetic drug" is unclear because a subject can respond positively or negatively to a drug. It is unclear what the expected outcome of the treatment would be if subjects are screened for their predisposition to "respond" to a drug.

7. Claims 4, 5, 6, and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4-6, and claims dependent therefrom, are directed to a method of identifying a patient sample in c clinical trial of a drug. The method comprises "identifying a patient..." and "determining the number of copies of apoE4 gene alleles." However the claims do not set forth the steps that would need to be taken to identify the patient and determine the number of apoE4 alleles in a subject.

Claim 6 also recites "said a disease." It is unclear, due to the apparent typographical error, whether Applicants are introducing another disease or whether they are referring to the "disease" of the preamble. Appropriate correction is required.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by POIRIER WO 95/29257 A2. POIRIER discloses a method identifying individuals afflicted with Alzheimer's disease that are predisposed to respond to therapy using a cholinomimetic drug. Specifically, such individuals are identified by the absence of an apolipoprotein E type 4 (ApoE4) isoform or DNA encoding ApoE4 in the subject(see Summary of the Invention). The absence of apoE4 gene alleles in an individual is indicative that that individual would be predisposed to respond to cholinomimetic based therapies (see page 15, lines 5-24). The reference also discloses the treatment of these individuals with the drug tacrine.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over POIRIER et al., Proc. Natl Acad. Sci. USA (1995) 92:12260-12264, and ROSES et al., US 5,508,167.

POIRIER et al. teaches that the absence of ApoE4 alleles in an individual would respond better to cholinergic drug therapies (see page 12263, first full paragraph). In particular, POIRIER et al. compares the responsive ness of individuals with and without ApoE4 alleles to the drug tacrine. However the reference does not teach a method of screening for the absence or presence of ApoE4 gene alleles.

ROSES et al. teaches a method of diagnosing or prognosing Alzheimer's disease in an individual that directly involves the detection of the presence or absence of an ApoE4 isoform or

DNA encoding ApoE4 in the subject (see Abstract). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have combined the teachings of POIRIER et al. and ROSES et al. to develop a method of screening for candidates who would benefit from treatment with a cholinomimetic drug.

Conclusion

12. No claims are allowed.

13. This is a Continued Prosecution Application of applicant's earlier Application No. 09/342,993. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Tu whose telephone number is 703-308-3968. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 703-308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER

ST
April 11, 2001